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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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EXAMINER	
CHERNYSHEV, OLGA N	

ART UNIT	PAPER NUMBER
1646	

DATE MAILED: 07/03/2003

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Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application N .	Applicant(s)	
	09/826,290	DURHAM ET AL.	
	Examiner	Art Unit	
	Olga N. Chernyshev	1646	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *05 May 2003* .

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *56-73* is/are pending in the application.

4a) Of the above claim(s) *56-67,72 and 73* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *59-67 and 73* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other:

DETAILED ACTION

Response to Amendment

1. Claims 51-55 have been cancelled, claims59, 60 and 63 have been amended as requested in the amendment of Paper No. 17, filed on May 05, 2003.

The numbering of newly presented claims 68-69 is not in accordance with 37 CFR 1.126 which requires the original numbering of the claims to be preserved throughout the prosecution. When claims are canceled, the remaining claims must not be renumbered. When new claims are presented, they must be numbered consecutively beginning with the number next following the highest numbered claims previously presented (whether entered or not).

Misnumbered claims 68 and 69 have been renumbered 72 and 73, respectively.Claims 56-73 are pending in the instant application.

Claims 56-58 and 68-71 have been withdrawn from further consideration pursuant to 37 CFR 1.142(b), as being drawn to invention nonelected by original presentation, there being no allowable generic or linking claim. See reasons of record in section 2 of Paper No. 15.

Claims 59-67 and 72-73 are under examination in the instant office action.

2. The Text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

3. Any objection or rejection of record, which is not expressly repeated in this action has been overcome by Applicant's response and withdrawn.

4. Applicant's arguments filed on May 05, 2003 have been fully considered but they are not deemed to be persuasive for the reasons set forth below.

Election/Restrictions

5. Applicant's continued traversal of the restriction requirement is not timely and, therefore, has not been considered.

Specification

6. The instant disclosure stands objected to for reasons of record in section 3 of Paper No. 15. Applicant argues that hyperlinks are permissible in the specification (see page 4, last paragraph of the Response) and refers to MPEP § 608.01. However, Applicant is reminded that MPEP § 608.01 clearly states that hyperlinks cannot be active in order to be properly presented. Appropriate correction is required.

7. Applicant is reminded about proper use of trademarks, see section 3 of Paper No. 15. It appears that, contrary to Applicant's statement on page 5, second paragraph of the Response, no amendment to capitalize trademarks in the instant specification has been made.

Claim Rejections - 35 USC § 112

8. Claims 59-67 and 72-73 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention for reasons of record as applied to claims 51-55 and 59-67 in section 5 of Paper No. 15.

Applicant submits that the data regarding the association between API-6 and Alzheimer's disease was first disclosed in the instant specification and, therefore, no support of such association can be found in the prior art. Applicant further refers to the Declaration of Soares under 37 CFR 1.132, which presents further data regarding the decrease of API-6 in a CSF sample of a patient with Alzheimer's disease. Applicant's arguments have been fully considered but are not deemed to be persuasive for the following reasons.

In determination whether a disclosure complies with 35 U.S.C. 112, first paragraph, enablement requirement, the factor regarding the state of the prior art has to be considered to estimate the amount of guidance necessary to be present in the specification. *In re Wands*, 8 USPQ2d, 1400 (CAFC 1988). Thus, because there is no reference of record found in prior art that would associate API-6 with Alzheimer's disease, one skilled in the art would have to rely solely on the information disclosed in the instant specification in order to practice the full scope of the instant invention. The Examiner maintains the position that the instant specification, as filed, fails to provide any evidence or sound scientific reasoning that would support a conclusion that the polypeptides of SEQ ID NOs: 36-39 are associated with Alzheimer's disease. While it is not necessary that Applicant understands or discloses the mechanism by which the invention functions, in this case, in the absence of such an understanding, no extrapolation can be made of the single point data, such as 1.30 fold decrease of AF-21 in CSF of subjects with Alzheimer's disease as compared to control values, to other "biological samples" (see claim 59), or to the "decreased level" in general.

Applicant argues that "in order to practice the claimed invention, one skilled in the art need only to detect a decrease in API-6 relative to a control sample or a reference range" (page 7,

first paragraph of the Response). However, the instant specification does not provide the essential information regarding how to estimate what level of decrease of API-6 can be considered sufficient to be diagnostic of Alzheimer's disease. A skilled practitioner readily understands that some deviation in any measurable feature exists among normal population. It is not clear and not disclosed in the instant specification, as filed, what the critical level of difference in API-6 is , which is indicative of Alzheimer's disease. It appears that the only numerical information regarding the level of decrease is presented in Table I, page 12, that AF-21 (which corresponds to API-6), which states that AF-21 was 1.30 fold decreased in CSF of subjects with Alzheimer's. Moreover, the instant specification clearly lacks guidance on the subject how to correlate API-6 values with the "degree of Alzheimer's disease" or "risk of developing Alzheimer's disease", as encompassed by claim 59.

The Declaration of Soares under 37 CFR 1.132 filed May 05, 2003 was fully considered but is insufficient to overcome the instant rejection. The declaration presents additional data obtained on one Alzheimer's disease patient, subject A, whose CSF was monitored for the presence of API-6. It is clear that the level of API-6 was decreased in CSF samples of that particular patient as compared to API-6 levels in control subjects. However, the question regarding the "reference range", as a comparison for "a decreased level" remains unanswered.

While the skill level in the art is high, the level of predictability is low. The sole information regarding the level of decrease (1.30 fold compare to normal control) presented in the specification, as originally filed, pertains to the CSF sample. One skilled in the art would not reasonably consider that this single example is predictive of API-6 in any biological sample of the subject suffering from Alzheimer's disease.

Applicant's invention is predicated on the finding that CSF samples of subjects with Alzheimer's disease, treated according to the disclosed protocol, contain API-6 at the level 1.30 fold decreased as compared to normal control. Applicant further extrapolates this result into a method for screening, diagnosis, or prognosis of Alzheimer's disease. Accordingly, it would appear that Applicant provides a single finding (the finding), and then presents an invitation to experiment to determine if other biological samples contain API-6, if API-6 are decreased in other biological samples of subjects with Alzheimer's disease, and what is the level of decrease that is indicative of the diagnosis of Alzheimer's disease.

A patent is granted for a completed invention, not the general suggestion of an idea and how that idea might be developed into the claimed invention. In the decision of *Genentec, Inc, v. Novo Nordisk*, 42 USPQ 2d 100,(CAFC 1997), the court held that:

"[p]atent protection is granted in return for an enabling disclosure of an invention, not for vague intimations of general ideas that may or may not be workable" and that "[t]ossing out the mere germ of an idea does not constitute enabling disclosure". The court further stated that "when there is no disclosure of any specific starting material or of any of the conditions under which a process is to be carried out, undue experimentation is required; there is a failure to meet the enablement requirements that cannot be rectified by asserting that all the disclosure related to the process is within the skill of the art", "[i]t is the specification, not the knowledge of one skilled in the art, that must supply the novel aspects of an invention in order to constitute adequate enablement".

The instant specification is not enabling because one can not following the guidance presented therein and practice the claimed method without first making a substantial inventive contribution.

New grounds of rejection necessitated by amendment

6. Claim 63 is rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. Claim 63 is vague and indefinite in so far as it employs the term "NCAM" as a limitation. The full name of this abbreviation should be presented at the first appearance of the term. Furthermore, it is not clear what "other members of the NCAM gene family" are encompassed by the claim.

Double Patenting

7. Applicant is advised that should claim 59 be found allowable, claims 71 and 72 will be objected to under 37 CFR 1.75 as being a substantial duplicate thereof. When two claims in an application are duplicates or else are so close in content that they both cover the same thing, despite a slight difference in wording, it is proper after allowing one claim to object to the other as being a substantial duplicate of the allowed claim. See MPEP § 706.03(k).

Claim 59 is directed to a method for screening, diagnosis, or prognosis of Alzheimer's disease by detecting API-6, wherein a decreased level of said API-6 relative to a control sample indicates the presence or degree of Alzheimer's disease. Thus, claim 59 obviously encompasses a method of quantitative detection of API-6 as compared to control or a previously determined

reference range. Therefore, claims 71 and 72, reciting the same limitations are considered to be covering "the same thing despite a slight difference in wording".

Conclusion

8. No claim is allowed.

9. **THIS ACTION IS MADE FINAL.** Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Olga N. Chernyshev whose telephone number is (703) 305-1003. The examiner can normally be reached on Monday to Friday 9 AM to 5 PM ET.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Yvonne Eyler can be reached on (703) 308-6564. The fax phone numbers for the

organization where this application or proceeding is assigned are (703) 782-9306 for regular communications and (703) 782-9307 for After Final communications.

Certain papers related to this application may be submitted to Technology Center 1600 by facsimile transmission. Papers should be faxed to Technology Center 1600 via the PTO Fax center located in Crystal Mall 1 (CM1). The faxing of such papers must conform with the notices published in the Official Gazette, 1156 OG 61 (November 16, 1993) and 1157 OG 94 (December 28, 1993) (see 37 C.F.R. § 1.6(d)0. NOTE: If Applicant *does* submit a paper by fax, the original signed copy should be retained by Applicant or Applicant's representative. NO DUPLICATE COPIES SHOULD BE SUBMITTED so as to avoid the processing of duplicate papers.

Official papers filed by fax should be directed to (703) 308-4556 or (703) 308-4242. If either of these numbers is out of service, please call the Group receptionist for an alternative number. Faxed draft or informal communications with the examiner should be directed to (703) 308-0294. Official papers should NOT be faxed to (703) 308-0294.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (703) 308-0196.

Olga N, Chernyshev, Ph.D.
July 2, 2003

JOHN ULM
PRIMARY EXAMINER
GROUP 1600